Protein transduction of transcription factors: a non-genetic approach to generate new pluripotent cell lines from human skin.

Grant Award Details

Protein transduction of transcription factors: a non-genetic approach to generate new pluripotent cell lines from human skin.

Grant Type: New Cell Lines

Grant Number: RL1-00644

Investigator:

Name:	Steve Dowdy
Institution:	University of California, San Diego
Type:	PI

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $1,073,585

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Protein transduction of transcription factors: a non-genetic approach to generate new pluripotent cell lines from human skin.

Public Abstract:

More than 100,000 patients await for organ transplants nationwide this year. The ground-breaking discovery of new pluripotent human stem cell lines (iPS) derived from skin fibroblasts using a core of 3-5 transcription factors opens the door to patient-derived pluripotent stem cells and new approaches to organ and tissue replacement. Patient-derived stem cells could have an immediate impact on hundreds of other medical applications and discoveries. A major bottleneck in translating these breakthroughs into the clinic is that pre-existing mutations in patients and mutations acquired from viral and DNA vectors pose a potential risk for cancer. To overcome this obstacle, we propose an alternative approach to generating patient-derived stem cell lines using cell-permeable, pluripotent-inducing transcription factors. Introducing active proteins into cells avoids the long-term risk of genetic mutations. Over the past 10 years, our labs have pioneered this technology to introduce over 50 functional proteins in a wide spectrum of human and animal cell types. First, we will use this technology to determine the optimal number of cell-permeable proteins necessary to induce pluripotency in human cells. Second, to reduce the risk of pre-existing cancer mutations, we will identify which cells in the human body are the best source to generate mutation-free patient stem cells. These two advances will help us reach our goal of developing new medical therapies for an endless list of diseases using patient stem cells.

Statement of Benefit to California:

Almost 20,000 Californians await organ transplants. The possibility of translating pluripotent stem cell technology to patient-derived stem cells could drastically improve the outlook for organ and tissue replacement therapy in the future. Hundreds of potential medical therapies and inventions using induced-pluripotent stem cells are limited because current approaches rely on DNA technology and cause mutations. Over the past 10 years, our labs have pioneered alternative non-DNA approach, which could introduce pluripotent-inducing transcription factors into cells without causing mutations. We have used this approach to introduce more than 50 active proteins into a broad spectrum of human and animal cell types. In this proposal, we will use this alternative non-genetic approach to induce pluripotent stem cells from human fibroblasts and to identify which human cell types are the best candidates for generating mutation-free patient-derived stem cells. These breakthroughs could have an immediate impact on medical treatments for Californians who are suffering from end-organ damage or have endocrine, neurological, and cardiac disease. Furthermore, these technologies will have an immense economic benefit to California by removing a major obstacle for biotechnology and pharmaceutical companies in California and giving California a leading edge in developing new treatments.
